Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

Mepolizumab

(non-sponsored review)

Indication: Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Aug 16, 2024

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Canada's Drug Agency – L'Agence des médicaments du Canada

Re: DRAFT Reimbursement Recommendation – Mepolizumab

As a patient organization, we are pleased to note the unanimous 6 to 0 vote, in deliberation, of the FMEC that rightly concluded Mepolizumab at the dose of 300 mg every 4 weeks addresses several unmet needs and achieves important outcomes for persons with eosinophilic granulomatosis with polyangiitis (EGPA), and specifically improved remission rates and reductions in OCS (oral corticosteroid) exposure.

However, in conversation with Craig Taylor we are both frustrated that the FMEC added the Table 2 Conditions, that mirror the MIRRA and MANDARA trials, meaning all EGPA patients must relapse or have refractory EGPA before gaining access to Mepolizumab. We feel**, the findings of MIRRA justify not restricting mepolizumab access to only those EGPA patients with relapsing or refractory EGPA.** In fact, the MIRRA results found 81% of patients in the placebo group did not have a remission compared to 47% on Mepolizumab, which also allowed for reduced OCS. **Clearly, these are key MIRRA findings to be reflected in the Table 2 Conditions**, and this result is already in a disadvantaged group of EGPA patients who have relapsed or have been deemed refractory.

Like Craig, **we don't want EGPA patients to experience a relapse or end up with refractory EGPA**, with all of the costs, risks, and other problems associated with these negative outcomes. We feel strongly that EGPA relapses should, and can, be avoided in 47% of patients by adding mepolizumab early to standard of care treatment rather than waiting for the 81% chance of relapsing, or becoming refractory, or worse! We also note there was **no significant safety difference** between the MIRRA Mepolizumab and placebo groups. **Craig, like all patients, wanted to reduce his exposure to OCS, but also to other immune suppressing agents** with known toxic side-effects, **MIRRA achieved this.**

We strongly believe the Table 2 Conditions should be amended as follows: "*Mepolizumab should be reimbursed in persons with a diagnosis of EGPA and who meet **either of** the following condition(s):…".* This small change aligns with the key MIRRA findings and needs to be reflected in Table 2. **Why impose the conditions of MIRRA, but not reflect the key findings of MIRRA?**

We also want to note, the Reimbursement Condition of a price reduction may be necessary compared to current Standard of Care medications that are more than 50 years old! Patients are tired of hearing such arguments in the context of life-threatening and rare diseases and expect pricing will be compatible to a basket of 13 countries which apparently no longer includes the US or Switzerland.

New treatments cost more because they do more, just like other modern technologies including computers or cars. Practically no one uses a 10 or 15 year-old car or computer so why are we comparing medical treatments which are about 5 times the age noted above?

In addition, as we all know, the MANDARA trial revealed that Benralizumab was shown to be non-inferior to Mepolizumab and is reported to be less expensive. We understand Benralizumab Health Canada approval is estimated in early 2025. I am sure someone will want to make a cost comparison between these two treatments!

As an organization, we are not happy that it is now more than 7 years post the MIRRA study and we in Canada are only addressing the access and reimbursement questions in late 2024. There are many reasons for this lag in time, but for patients in need of care it is another example of Canada's healthcare system failing they very Canadian patients it supposed to be serving. EGPA patients in Canada have been denied access to Mepolizumab, a targeted EGPA treatment and the only HC approved treatment, for far too long, period.

We also know other patients in the arthritis community get access, and have had access, and coverage to other expensive biologics like Enbrel or Erelzi which carry ongoing costs of +/- thousands per month. And, if we dare to compare EGPA treatments to cancer treatments the inequality in access and reimbursement is even more shocking. I personally know a friend in Ontario receiving Imbruvica, or Ibrutinib, at a monthly cost of 11,400.00 per month for leukemia care. **EGPA patients, and other vasculitis patients, deserve a more equal access to care.**

Finally, the number EGPA patients in Canada is small with the estimated number of patients eligible for Mepolizumab to be in the range of 200 to 500 maximum, and many of those we expect, based on the onset age of EGPA, will have private insurance coverage.

EGPA is a rare disease, and we must make up for lost time and get access and reimbursement to Mepolizumab resolved as quickly as possible.

Yours sincerely,

Jon Stewart
President, Vasculitis Foundation Canada

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SX0839
Name of the drug and Indication(s)	mepolizumab
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	X
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	☐
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Page 9, Full Rec, Table 2, reimbursement condition: • Prednisone or a steroid equivalent to prednisone 7.5mg/day or above? • Due to the substantial cost difference of mepolizumab vs other immunosuppressive therapies, as well as cyclophosphamide and rituximab - is there any implementation guidance that jurisdictions may ask for a trial of prior immunosuppressive agents such as cyclophosphamide, rituximab, azathioprine, methotrexate, etc? **Page 9, Full Rec, Table 2,** Discontinuation criteria: In the "Policy Considerations for Reimbursing the Drug" in the "FMEC Responses to Drug Programs" A clinical expert response note that anticipated duration of therapy may vary. For implementation, do jurisdictions have the ability to ask for the treatment plan of mepolizumab

(i.e., consideration of tapering to 100mg every 4 weeks or weaning off therapy if on mepolizumab for more than 5 years)?
c) Implementation guidance
Full rec, Table 2 prescribing: would it be possible to highlight the specialties (i.e., rheumatologists, respirologists, internal medicine specialists)? **Full rec, Table 2** cost: is it possible to note transparently the large budget impact? Guidance is needed regarding: - How relapsing and refractory EGPA are defined for purposes of therapy initiation - What the initial duration of therapy should be prior to the initial renewal assessment ("at least 26 weeks" is imprecise and will cause problems with adjudication) - How often patients should be monitored to assess for continued benefit after the initial renewal assessment, and how sufficient benefit to continue therapy is defined

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SX0839
Brand name (generic)	NUCALA (mepolizumab)
Indication(s)	Eosinophilic granulomatosis with polyangiitis (EGPA)
Organization	GlaxoSmithKline Inc.
Contact information[a]	Name: [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

Under Table 1: Economic Implications, "The absence of evidence for long-term treatment benefits of mepolizumab beyond 52 weeks limits the availability of data needed to assess its cost-effectiveness."

There is evidence from open-label extension studies and real-world evidence that extend beyond 52 weeks showing mepolizumab effectiveness is sustained over the long-term. Given the rarity of this disease, we feel this evidence warrants consideration when discussing long-term efficacy and safety of mepolizumab in EGPA patients.

Evidence up to 24 months: Bettiol A, et al. *Arthritis Rheumatol* 2022;74:295–306
Evidence up to 7.4 years: Khoury P, et al. AAAAI 2024. Poster L35
Evidence up to 7.4 years: Ishii T, et al. *Annals of the Rheumatic Diseases* 2024;83:385-386.

Overall, we acknowledge CDA's position on limitations in assessing cost-effectiveness, but we believe the words "absence of evidence" do not acknowledge the aforementioned studies and should be changed to "some evidence" to reflect that evidence does exist in this rare patient population demonstrating the long-term treatment benefits of mepolizumab beyond 52 weeks.

Secondly, GSK would like CDA to consider recognizing that the primary limiting factors in conducting a robust cost-effectiveness analysis are the inherent heterogeneity of the EGPA population and uncertainties in disease modeling due to its rarity, rather than primarily the limitations in long-term

evidence. The rarity and complexity of EGPA result in limited data in epidemiology, healthcare resource utilization, and costs, making economic evaluations particularly challenging.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

Reimbursement conditions requiring clarification	CDA's rationale	Manufacturer's response
Under Table 2: Discontinuation Criteria Mepolizumab should be discontinued after a trial of at least 26 weeks therapy if there is no clinical improvement as demonstrated by one of the following: - inability to reduce the daily dosage of prednisone by 50% or - inability to reduce the daily dosage of prednisone below 7.5 mg/day or - if there is a consistent recurrent need to increase or resume oral corticosteroid therapy	Treatment should be continued for at least 26 weeks, at which time effectiveness should be assessed. Expert opinion suggests that mepolizumab therapy must demonstrate a benefit and/or a reduction in the dosing of concomitant OCS administration to qualify for renewal. The recurrent need to increase or resume oral corticosteroid therapy constitutes a treatment failure according to the clinical experts.	1) We are aligned with the criteria outlined by CDA and request a minor language update for clarity. Instead of "below 7.5mg", kindly update the language to "at or below 7.5mg". This wording more accurately captures patients using the 7.5mg dose format. 2) In the implementation guidance, CDA acknowledges that use of mepolizumab may include reducing the use of immunosuppressive therapies. We feel that this is indicative of significant clinical benefit if achieved at 26w and should be added as a criterion within the reimbursement conditions. This additional criterion would be relevant in the scenario whereby a patient is able to reduce their use of immunosuppressive therapy by 26w but does not reach the 50% or 7.5mg threshold of OCS reduction. In this case, the patient would have received significant clinical benefit, but would need to discontinue mepolizumab based on the current draft criteria. We suggest including another point in the discontinuation criteria, e.g. "OR inability to discontinue or reduce the dosage of immunosuppressive medication", to define when this patient should continue/ discontinue treatment.

[a] CADTH may contact this person if comments require clarification.